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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/832,443	Applicant(s) Wolpe et al
	Examiner Julie E. Reeves, Ph.D.	Group Art Unit 1642

Responsive to communication(s) filed on _____.

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *zero* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *1-90* _____ is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) _____ is/are rejected.

Claim(s) _____ is/are objected to.

X Claims *1-90* _____ are subject to restriction or election requirement.

Application Papers

X See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

SEE OFFICE ACTION ON THE FOLLOWING PAGES

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-8, drawn to a polypeptide comprising a hemoglobin alpha chain, a pharmaceutical composition containing the polypeptide, classified in class 530, subclass 385, for example.

II. Claims 9-10, and claims 47-49, in part, drawn to a method of inhibiting stem cell proliferation comprising contacting hematopoietic cells with a peptide of group I, classified in class 514, subclass 2. Claims 47-49 will be examined with group II to the extent that they read upon administering INPROL peptides in the absence of an opiate compound.

III. Claim 11, drawn to a method of stimulating the growth of B cells by administrating the polypeptide of group I, classified in class 514, subclass 2.

IV. Claims 12-16, and claims 62-65, in part, drawn to a method of treating cancer by administrating the polypeptide of group I, classified in class 514, subclass 2. Group IV will be examined to the extent that claims 62-65 read upon the administration of an opiate

V. Claims 17-18, drawn to a method of treating cancer by administrating the polypeptide of group I ex vivo, classified in class 514, subclass 2.

VI. Claims 19-21, drawn to a method of inhibiting stem cell division in a mammal by administrating the polypeptide of group I, classified in class 514, subclass 2.

VII. Claims 22-24, and Claims 69-70, in part, drawn to a method of maintaining stem cell division ex vivo by administrating the polypeptide of group I, classified in class 514, subclass 2. Claims 69-70 will be examined with Group VII to the extent that they read upon the administration of the INPROL peptide in the absence of an opiate compound.

VIII. Claims 25-26, and Claims 72-73, in part, drawn to a method of treating myleoproliferating or autoimmune disease or epithelial stem cell hyper proliferation by administrating the polypeptide of group I, classified in class 514, subclass 2. Claims 72-73 will be examined with Group VIII to the extent that the claims read upon the administration of the INPROL peptide in absence of the opiate compound.

IX. Claims 27-29, drawn to a method of protecting stem cells and not cancer in a mammal from chemotherapy or radiation by administrating the polypeptide of group I, classified in class 514, subclass 2.

X. Claim 30, drawn to a method of vaccinating by administrating the polypeptide of group I, classified in class 424, subclass 533.

XI. Claim 31, drawn to a method of treating immunodepression by administrating the

XII. Claims 32-33, and Claim 80, in part, drawn to a method of conducting gene therapy, classified in class 514, subclass 44. Claim 80 will be examined with Group XII to the

extent that it reads upon the administration of the INPROL peptide is in absence of the opiate compound.

XIII. Claims 36-38, and claims 82-83, in part, drawn to a method of conducting ex vivo stem cell expansion by contacting hematopoietic cells with the polypeptide of group I, classified in class 514, subclass 2. Claims 82-83 will be examined with Group XIII to the extent that they read upon the administration of the INPROL peptide in absence of the opiate compound.

XIV. Claims 39-40, drawn to a composition comprising the polypeptide of group I and an inhibitory compound, classified in Class 424, subclass 85.1. It is noted that claim 40 recites the apparent typographical error of "a method as in claim 39". This phrase is being interpreted as "the pharmaceutical composition of claim 39" for the purposes of restriction. It is suggested that Applicant review the claim language and make any appropriate amendments in response to this action.

XV. Claims 41-42, drawn to a composition comprising the polypeptide of group I and an stimulatory compound, classified in Class 424, subclass 85.2.

XVI. Claims 43-45, drawn to a method for expressing alpha hemoglobin or substitution or deletion analogs thereof, classified in class 435, subclass 69.6.

class 530, subclass 300

XVIII. Claims 47-52, in part, drawn to a method of stimulating stem cell proliferation comprising contacting hemopoietic cells with INPROL and an opiate compound, classified in class 530, subclass 300, for example. It is noted that claim 47 text is missing from the last part of the first line due to the page being folded over during photocopying. For the purposes of this restriction requirement, the claims is being interpreted as "...comprising contacting...". Appropriate amendment is suggested. Group XVII will be examined to the extent that it reads upon administration of an INPROL peptide in the absence of an opiate compound.

XIX Claims 47-52, in part, drawn to a method of stimulating stem cell proliferation comprising contacting hemopoietic cells with an opiate compound, classified in class 530, subclass 300, for example. Group XIX will be examined to the extent that it reads upon administration of an opiate compound in the absence of an INPROL peptide.

XX. Claims 53-57, drawn to a method of stimulating or inhibiting stem cell proliferation comprising contacting hematopoietic cells with a compound capable of activating the G inhibitory subclass of GTP binding proteins or capable of binding nociceptin receptors, classified in class 530, subclass 300, for example, if the compound is a small peptide.

XXI Claims 58-59, drawn to a method of identifying a receptor for INPROL comprising a

XXII Claims 60-61, drawn to a method for identifying a receptor for INPROL comprising a adenylate cyclase assay, classified in class 435, subclass 183.

XXIII. Claims 62-65, in part, drawn to a method of treating cancer comprising administering INPROL and an opiate compound , classified in class 514, subclass 2, for example. Claims 62-65 will be examined in Group XXIII to the extent that claims 62-65 read upon the administration of both INPROL and an opiate compound.

XXIV. Claims 62-65, in part, drawn to a method of treating cancer comprising administering an opiate compound , classified in class 514, subclass 2, for example. Claims 62-65 will be examined in Group XXIV to the extent that claims 62-65 read upon the administration of an opiate compound in absence of INPROL peptides.

XXV. Claims 66-68, in part, drawn to a method of stimulating stem cell division by administering INPROL peptide and an opiate compound, classified in class 514, subclass 2. Claims 66-68 will be examined in Group XXV to the extent that they read upon administration of both an INPROL peptide and an opiate compound.

XXVI. Claims 66-68, in part, drawn to a method of stimulating stem cell division by administering an opiate compound, classified in class 514, subclass 2. Claims 66-68 will be examined with Group XXVI to the extent that they read upon administration of an opiate compound in absence of INPROL peptides

administering INPROL peptide and an opiate compound, classified in class [illegible].

subclass 2. Claim 66 will be examined in Group XXVII to the extent that it reads upon administration of an INPROL peptide in the absence of an opiate compound.

XXVIII. Claims 69-71, in part, drawn to a method of maintaining mammalian hematopoietic stem cells ex vivo by administering INPROL peptide and an opiate compound, classified in class 514, subclass 2. Claims 69-71 will be examined with Group XXVIII to the extent that they read upon administration of both an INPROL peptide and an opiate compound.

XXIX. Claims 69-71, in part, drawn to a method of method of maintaining mammalian hematopoietic stem cells ex vivo administering an opiate compound, classified in class 514, subclass 2. Claims 69-71 will be examined with Group XXIX to the extent that they read upon administration of an opiate compound in absence of INPROL peptides.

XXX. Claims 72-74, in part, drawn to a method of method of treating myleoproliferating or autoimmune disease or epithelial stem cell hyper proliferation by administrating INPROL peptide and an opiate compound, classified in class 514, subclass 2. Claims 72-74 will be examined with Group XXX to the extent that they read upon administration of both an INPROL peptide and an opiate compound

or autoimmune disease or epithelial stem cell hyper proliferation by administering an opiate compound, classified in class 514, subclass 2. Claims 72-74 be examined

with Group XXXI to the extent that they read upon administration of an opiate compound in absence of INPROL peptides.

XXXII. Claims 75-76, in part, drawn to a method for treating or preventing stem cell exhaustion by administering INPROL peptides, classified in class 514, subclass 2, for example. Claims 75-76 will be examined in Group XXXII to the extent that they read upon the administration of INPROL peptide in absence of an opiate compound.

XXXIII. Claims 75-77, in part, drawn to a method for treating or preventing stem cell exhaustion by administering INPROL peptides and an opiate compound, classified in class 514, subclass 2, for example. Claims 75-77 will be examined in Group XXXIII to the extent that they read upon the administration of both the INPROL peptide and an opiate compound.

XXXIV. Claims 75-77, in part, drawn to a method for treating or preventing stem cell exhaustion by administering an opiate compound, classified in class 436 subclass 92, for example. Claims 75-77 will be examined in Group XXXIV to the extent that they read upon the administration of an opiate compound in the absence of an INPROL peptide

from chemotherapy or radiation by administering a opiate compound, classified in

class 436, subclass 92

XXXVI. Claims 80-81, in part, drawn to a method of gene therapy by treating ex vivo with INPROL and an opiate compound, classified in class 514, subclass 2 and class 436, subclass 92, for example. Claims 80-81 will be examined with Group XXXVI to the extent that they read upon the administration of both INPROL peptide and the opiate compound.

XXXVI. Claims 80-81, in part, drawn to a method of gene therapy by treating ex vivo with INPROL and an opiate compound, classified in class 436, subclass 92, for example. Claims 80-81 will be examined with Group XXXVI to the extent that they read upon the administration of the opiate compound in absence of the INPROL peptides.

XXXVII. Claims 82-84, in part, drawn to a method of conducting ex vivo stem cell expansion comprising contacting hematopoietic cell with a stimulatory amount of INPROL peptide and an opiate compound, classified in class 514, subclass 1 and class 436, subclass 92, for examples. Claims 82-84 will be examined with Group XXXVII to the extent that they read upon the administration of both the INPROL peptides and the opiate compound.

XXXVIII Claims 82-84, in part, drawn to a method of conducting ex vivo stem cell

an opiate compound, classified in subclass 92, for example. Claims 82-84 will be

examined with Group XXXVIII to the extent that they read upon the administration of the opiate compound in absence of the INPROL peptide.

XXXIX. Claim 85, drawn to a pharmaceutical composition comprising an opiate compound and an inhibitory compound, classified in class 436, subclass 92, for example.

XXXX. Claim 86, drawn to pharmaceutical composition comprising an opiate compound and an stimulatory compound, classified in class 436, subclass 92, for example.

XXXXI. Claims 87-88, drawn to a method of treating pain by administering INPROL peptide, classified in class 514, subclass 2.

XXXXII. Claims 89-90, drawn to a method of treating immune deficiency by administering INPROL peptide, classified in class 514, subclass 2. It is noted that claims 89-90 on pages 125-126 of the specification were originally incorrectly numbered as claims 87-88. Under Rule 126, claims 87-88, second occurrence have been renumbered as claims 89-90. Accordingly, for the purposes of examination, dependent renumbered claim 90 is being interpreted as being dependent upon renumbered claim 89. Appropriate amendment is suggested.

2. The inventions are distinct, each from the other because of the following reasons:

which are made by materially different methods, and are used in materially different methods [illegible] different modes of operation, different functions and different effects. In the instant

case the different inventions contain a hemoglobin alpha chain with no other compound (Invention I) or with a stimulatory compound (Invention XV) or with an inhibitory compound (Invention XIV), various peptides (Invention XVII), opiate compounds with an inhibitory compound (Invention XXXIX) or an opiate r compound with a stimulatory compound (Invention XXXX). These compositions will accordingly have different effects and different modes of operation. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus Inventions I, XIV and XV are patentably distinct.

3. The inventions are distinct, each from the other because of the following reasons: Inventions II-XIII, XVI, XVIII-XXXVII, and XXXXI-XXXXII differ in the method objectives, method steps and parameters and in the reagents used. In the instant case the different inventions relate to the treatment of a variety of different conditions (autoimmunity, cancer, stimulating growth of B cells, inhibiting stem cell division, to list a few as examples. See each of the different groups listed above. The examination of all groups would require different searches in the U.S. PATENT shoes and the scientific literature and would require the consideration of different patentability issues. Thus Inventions II-XIII are separate and distinct in having different method steps and different endpoints and are patentably distinct.

XXXXII are related as products and processes of use. The inventions can be shown to be [illegible] of the other or both of the following can be shown: (1) the process for using the product as

claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the products cen be used for a variety of different products, as recited in the various methods claimed. Thus Inventions I, XIV and XV and Inventions II-XIII, XVI, XVIII-XXXVII, and XXXXI-XXXXII are patentably distinct.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, and because of their recognized divergent subject matter, particularly for the various treatments and methods recited in the claims, which raise different issues of administration, pathology, and other medically related issues, restriction for examination purposes as indicated is proper.

6. This application contains claims directed to the following patentably distinct species of the claimed invention:

7. For the groups that refer to the polypeptide of group I, an election of species is set forth between

Species A: wherein the C-terminal hydrophobic domain (amino acids 98-141) has been substituted or deleted, and

Species B: wherein the C-terminal haptoglobin-binding domain (amino acids 121-127) has

Species C: amino acids 1-97 of human hemoglobin chain and

Species D: amino acids 1-94 of human hemoglobin chain

The deletion of the various domains will affect the structure of the resulting proteins, which in turn, will affect the biological, immunological and therapeutic function of these proteins The loss of amino acids 95-97 will affect the structure of the resulting proteins, which in turn, will affect the biological, immunological and therapeutic function of these proteins.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-90 are generic.

8. If group VIII, XXX or XXXI is chosen, an election of species is set forth between

Species E: myeloproliferative disease

Species F: autoimmune disease

Species G: Epithelial stem cell hyper proliferation

Not all autoimmune disease are caused by myeloproliferative diseases or by epithelial stem cell hyper proliferative. Conversely, not all autoimmune disease results in stem cell hyper proliferation or in myeloproliferation. Finally, epithelial stem cell proliferation may result, for example, in cancer or the cervix, cancer of the skin, in addition to myeloproliferative diseases or [illegible] immunity. As the pathological and etiological agents for these three difference classes of

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 25-26 and 72-74 are generic.

9. If group II, IV, VII, VIII, XIII or XX is chosen, an election of species is set forth between The inhibitory or the stimulatory method or product.

The mechanisms or inhibition or stimulation are biologically and physiologically different and result in different end-points. Thus, the species are patentably distinct.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 53-57 are generic.

10. If either of Groups XIV or XXXIX is chosen, an election of species is set forth between

Species H: MIP-1 alpha

Species I-P: TGF beta and so forth through the tripeptide glutathione (Gly-Cys-

Gly) as recited in claims 39 and 85

different biological properties, the species are patentably distinct.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 39-40 and 85 are generic.

11. If either of Groups XV or XXXX is chosen, an election of species is set forth between

Species Q: IL-1

Species R-II: IL-2 and so forth through the flk2/flt3 ligand as recited in claims 41 and 86.

As each of these stimulators have different primary amino acid structure resulting in different biological properties, the species are patentably distinct.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 41-24 and 86 are generic.

12. If any of Groups II, XVII, XXI, XXII, XXXXI or XXXXII is chosen, an election of species is set forth between one of the four peptides recited in claim 46, or one of the fifteen peptides recited in claim 49, one of the seven peptides recited in claim 59 or 61 or one of the ten peptides recited in claims 88 and renumbered claim 90. As all of the seven peptides in claim 59 are repeated in either claims 46 or 49, they are not listed out separately.

Species II: Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val

As each of these peptides have different primary amino acid structure and different [illegible] different biological properties, the species are patentably distinct

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 47-49, 58-61, 88 and renumbered claim 90 are generic.

13. If any of Groups XVII, XIX, XXIII-XXXI, XXXIII-XXXX is chosen, an election of species is set forth between one of the twenty four opiate compounds as recited in claims 50, 65, 68, 71, 74, 77, 79, 81, 84.

Species ZZ-WWW: Morphine through nociceptin.

As each of these compounds have different structure, different modifications and different effects resulting in different pharmacological properties, the species are patentably distinct.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 47-52, 62-86 are generic.

Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

14. A telephone call was made to B.J. Sadoff on 1 Spetember 1998 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie E. Reeves, Ph.D. whose telephone number is (703) 308-7553.

September 1, 1998